(b) a second facilitator substance not chemically related to said first substance to aid in the infusion of the first substance into said at least one cell whose concentration is greater than 20% of the total composition,

wherein the concentrations of said first and second substances are effective to stabilize the nucleic acids of said at least one cell in a specimen at ambient temperature, and further wherein the combined concentration of said first and second substances is 100% of said composition.

REMARKS

Claims 1-4, 6-8, 10 and 12-17 are in the present application.

Claims 1-4, 6-8, 10 and 12-17 have been rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject matter not sufficiently described in the specification in such a way as to convey that the inventors had possession of the claimed invention. Applicants have amended Claim 1 in order to advance prosecution and further clarify the subject matter of the present invention. Claim 1 has been amended by addition of the phrase "not chemically related to said first substance" after the phrase "a second facilitator substance."

Applicants respectfully submit that the Examiner is incorrect in rejecting the present claims, based on the specification not teaching "the very large genus of claimed compositions". If one shows a range of concentration, from a low of 20% to a high of 80% and with points in between, and they all work as stated, then anyone skilled in science can very reasonably infer that all points between the two extremes will work. This is the nature of, for example, standard curves for analytical work. One constructs a standard curve by plotting discrete points on a dose-response graph and then connects the points. The resulting line or curve is then used to read off any concentration (the "dose") or response between the low and the high. Applicants respectfully submit that it is not scientifically reasonable to assume that in the case of the claimed compositions, there are concentrations between those actually described in the specification

samples by DNA probe binding to target sequences in the rRNA of the three organisms, the fact is that the Examples in the Specification show the efficacy of the claimed compositions in preserving this RNA sample. Example 11 proves that one way that preservation occurs is by protection against degradation. Example 11, taken with the other Examples in the Specification, strongly demonstrates that the compositions do penetrate these target cells and that nucleic acid is preserved in these cells, and that one mode of that preservation is by eliminating nuclease activity. So one of ordinary skill in the art takes the information from the Examples that these compositions preserve the RNA for detection by hybridization methods (e.g., Affirm VPIII).

Applicants respectfully submit that the Specification therefore does provide enough written description of the claimed composition as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. Accordingly, withdrawal of the present rejection under 35 U.S.C. §112 is respectfully requested.

The Examiner has rejected Claims 1, 2, 4, 8 and 13-16 under 35 U.S.C. §102(b) as allegedly anticipated by Evinger-Hodges as taught by Gee et al. and Morris. The presently claimed invention as amended is not anticipated by the cited prior art.

The Examiner states that the reference Evinger-Hodges et al. discloses a composition for nucleic acid stabilization composed of an alcohol and a facilitator. Evinger-Hodges et al. do not teach a facilitator. The term "facilitator" is not used in this reference. In fact, one skilled in the art would not consider acetic acid or acetone, for example (see page 13, lines 24-35), a facilitator as it is used in the presently claimed invention as amended. This appears to be an extrapolation by the Examiner. In the cited reference the combination of methanol-ethanol or methanol-acetone would be considered the first component of claim 1 of the presently claimed invention as amended ("...comprising **at least one alcohol or ketone**. . ."). not the first and second component. The fact that Gee et al.

teaches that acetone is a "facilitator" (Gee et al. actually uses the term "permeabilization" – col. 30, line 56, so once again, the Examiner is interpreting meaning) is rendered moot by the new claim language in Claim 1. Since acetone is a ketone, it could not serve as the "facilitator" component in the claimed invention as amended. Furthermore, Gee et al. teaches that "permeabilization" of large and bulky dye molecules are why acetone may be used. Nowhere in Gee et al., with or without Evinger-Hodges et al., is a preservative taught whose composition is that which is claimed in the present invention. Similarly, Evinger-Hodges et al. do not teach the composition claimed in the present invention, with or without Gee et al.

Although the claims have been rejected as anticipated under 35 U.S.C. §102(b) on the disclosure of Evinger-Hodges et al. in view of Gee et al. and Morris, it is axiomatic that anticipation under Section 102 requires that the prior art reference disclose every element of the claim. In re King, 801 F.2d 1324, 1326, 231 U.S.P.Q. 136, 138 (Fed. Cir. 1986). Thus there must be no differences between the subject matter of the claim and the disclosure of the prior art reference. Stated in another way, the reference must contain within its four corners adequate directions to practice the invention. The corollary of this rule is equally applicable. The absence from the reference of any claimed element negates anticipation. Kloster Speedsteel AB v. Crucible Inc., 793 F.2d 1565, 1571, 230 U.S.P.Q. 81, 84 (Fed. Cir. 1986)

Here is it clear that Claim 1 as amended and all claims dependent thereon differ from Evinger-Hodges et al. in view of Gee et al. and Morris. Clearly, Kloster Speedsteel shows that the cited art falls far short of the statutory standard of 35 U.S.C. 102(b). Claims 1, 2, 4, 8 and 13-16 are not anticipated by Evinger-Hodges et al. in view of Gee et al. and Morris. Withdrawal of the instant rejection under Section 102 is therefore respectfully requested.

The Examiner has alleged that Claims 3, 6, 7, 10, 12 and 17 are rendered obvious under 35 U.S.C. §103 by Gee et al. and Evinger-Hodges et al. The cited prior art does not teach or suggest the claimed invention.

The present invention describes a composition for stabilizing the nucleic acids of at least one cell in a specimen at ambient temperature, the composition being comprised of:

(a) a first substance capable of precipitating or denaturing proteins, comprising at least one alcohol or ketone whose concentration is less than 80% of the total composition; and

(b) a second facilitator substance not chemically related to the first substance to aid in the infusion of the first substance into said at least one cell whose concentration is greater than 20% of the total composition, wherein the concentrations of said first and second substances are effective to stabilize the nucleic acids of said at least one cell in a specimen at ambient temperature, and further, wherein the combined concentrations of said first and second substances is 100% of said composition.

Applicants respectfully submit that in view of Claim 1 as amended, acetone is not "claimed" as a facilitator. Thus neither Evinger-Hodges et al. nor Evinger-Hodges et al. in view of Gee et al. teach the claimed composition. Gee et al. may, in fact, teach a similar composition, as is stated by the Examiner, but they certainly do not teach the presently claimed composition. It is therefore, not reasonable for one skilled in the art to assume a formulation like that claimed in the present invention would be obvious, based on reading the cited references and focusing on their taught preservative **without experimental evidence that the particular formulation works**. As is obvious in Example 3, the commonly available preservatives, including some that are touted to work to preserve nucleic acids (e.g., "PreservCyt"), do not result in detectable nucleic acid by direct DNA probe methodology. Thus, formulations such as alcohol/acetic acid, etc., as taught in Evinger-Hodges et al. and/or Gee et al. can

be improved upon and do not reflect the composition claimed in the present invention.

It is well established that obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination, Carella v. Starlight Archery, 804 F.2d 1356, 231 U.S.P.Q. 644 (Fed. Cir. 1986). In determining obviousness, the inquiry is not whether each element existed in the prior art, but whether the prior art made obvious the invention as a whole for which patentability is claimed. Hartness International, Inc. v. Simplimatic Engineering Co., 189 F.2d 1100, 2 U.S.P.Q. 2d 1826 (Fed. Cir. 1987). Furthermore, the Examiner cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to depreciate the claimed invention, In re Fine, 837 F.2d 1071, 5 U.S.P.Q. 2d 1596 (Fed. Cir. 1988), which the Examiner has clearly done in order to reject the claims under 35 U.S.C. §103.

Applicants have carefully studied the cited art as applied by the Examiner to reject the present claims and respectfully assert that the cited art does not render the teachings of the present invention obvious to one of ordinary skill in the art. Therefore, it is believed that the rejections of the claims under 35 U.S.C. §103 is improper, and withdrawal of this rejection is respectfully requested.

In view of the above Amendments and Remarks, it is believed that the present application is in condition for allowance, which action is earnestly solicited. Attached hereto is a marked-up version of the changes made to the claim by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claim 1 has been amended as follows.

1. (4x Amended) A composition for stabilizing the nucleic acids of at least one cell in a specimen at ambient temperature, said composition being comprised of:

(a) a first substance capable of precipitating or denaturing proteins, comprising at least one alcohol or ketone whose concentration is less than 80% of the total composition; and

(b) a second facilitator substance not chemically related to said first substance to aid in the infusion of the first substance into said at least one cell whose concentration is greater than 20% of the total composition,

wherein the concentrations of said first and second substances are effective to stabilize the nucleic acids of said at least one cell in a specimen at ambient temperature, and further wherein the combined concentration of said first and second substances is 100% of said composition.